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EXAMINER	
HOWARD, ZACHARY C	

ART UNIT	PAPER NUMBER
1646	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/557,283	CHATTERJEE ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,8 and 39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6, 8 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 August 2010* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 8/2/10 has been entered in full. Claims 1-4 are amended. Claims 7, 9-11, 17, 29, 37 and 38 are canceled (claims 12-16, 18-28 and 30-36 were canceled previously). New claim 39 is added.

In view of Applicants' cancellation of all of the withdrawn claims of Groups II and III (claims 17, 19, 37 and 38), the restriction requirement between Group I and Groups II and III is currently moot, but will be reinstated if claims to the other groups are re-introduced in subsequent claim amendments.

Each of the pending claims reads on each of the three elected species (see pg 2 of the 4/30/09 Office Action).

Claims 1-6, 8 and 39 are pending and under consideration.

Withdrawn Objections and/or Rejections

The following page numbers refer to the previous Office Action (4/30/09).

The objections to the Drawings at pg 3 are *withdrawn* in view of the replacement sheets filed by Applicants on 8/2/10. The replacement sheet for Figure 7 labels the two portions as "A" and "B", in accord with the Brief Description of Figure 7 on page 8 of the specification. The replacement sheet for Figure 13 is correctly labeled "Fig. 13".

The objection to claim 1 at pg 4 is *withdrawn* in view of Applicants' amendments to the claim.

The rejection of claims 2-4 under 35 U.S.C § 112, second paragraph, at pg 5-6 for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is *withdrawn* in view of Applicants' amendments to the claims.

The rejection of claims 1-3 under 35 U.S.C. § 102(a) at pg 7-9 as being anticipated by Conde-Knape et al (2002) is *withdrawn* in view of Applicants' amendments to the claims. The claims are now limited to a subject that is human. The subjects of Conde-Knape et al are transgenic apoE-null/C-I created by crossing a "moderately overexpressing human apoC-I transgenic" and an "apoE-null mouse"

($ApoE_0$)(Abstract). While $ApoE_0$ mice represent a model for atherosclerosis due to hyperlipidemia, Conde-Knape et al do not teach that the $ApoE_0$CI mice are a particular model for any human population; this strain was instead created to test whether ApoCI acts primarily via interference with apoE-mediated lipoprotein uptake (see Abstract). Further, the increase in ApoCI levels in the $ApoE_0$CI mice was compared to $ApoE_0$ mice.

The rejection of claims 5 and 6 under 35 U.S.C. § 103(a) at pg 10-11 as being unpatentable over Conde-Knape et al (2002) is *withdrawn* in view of Applicants' amendments to the claims, for the same reasons as for the 102(a) rejection.

Maintained Objections and/or Rejections

Specification

The disclosure was objected to on grounds (1)-(4) at pg 3-4 of the 4/30/09 Office Action. Each ground is maintained, for the following reasons.

(1) The title of the invention was objected to for not being descriptive of the elected invention, which is directed to a method of determining risk of atherosclerosis-associated plaque rupture or myocardial infarction based on measuring the level of ApoCI in a sample from a subject. In the 8/2/10 response, Applicants have amended the title to "METHODS OF DIAGNOSING ATHEROSCLEROSIS". However, the amended title remains not descriptive of the elected invention because it is directed generally to any method of diagnosing atherosclerosis, whereas the claimed invention is limited to methods based on measuring ApoCI. A new title is required that is clearly indicative of the invention to which the claims are directed. The following titled is suggested "METHODS OF DIAGNOSING ATHEROSCLEROSIS BY MEASURING APOCI".

(2) A corrected priority statement of the instant application's parent provisional and nonprovisional applications should be included in the first sentence of the specification or application data sheet. Specifically, the priority statement should indicate that the application is a 371 of PCT/US04/16419. The ADS filed 11/30/06 incorrectly indicates that the instant application is a Continuation of PCT/US04/16419.

Applicants' responses filed on 10/29/09 and 8/2/10 do not contain any reference to this objection. Neither the specification, nor the ADS, has been amended to correct this information.

(3) The description of Figure 9 begins "Figures 9A-9O depict…", whereas Figure 9 has parts A-P. The description does subsequently refer to Figure 9P (line 6 on pg 9), but for clarity the Brief Description of Figure 9 should start "Figures 9A-9P depict..."

Applicants' responses (10/29/09 and 8/2/10) do not contain any reference to this objection. The specification has not been amended to correct this information.

(4) The Brief Description of Figure 12 (pg 12) does not contain a reference to each of parts A-D shown in the Figure. See 37 CFR § 1.74, which states “When there are drawings, there shall be a brief description of the several views of the drawings and the detailed description of the invention shall refer to the different views by specifying the numbers of the figures and to the different parts by use of reference letters or numerals (preferably the latter)” and MPEP 601.01(g) which states “if the drawings show Figures 1A, 1B, and 1C and the brief description of the drawings refers only to Figure 1, this is an error in the specification which must be corrected.”

Applicants' responses (10/29/09 and 8/2/10) do not contain any reference to this objection. The specification has not been amended to correct this information.

Appropriate correction is required.

Application Data Sheet

An ADS was filed on 11/30/06 that includes incorrect "Domestic Priority Information". Specifically, the ADS incorrectly indicates that the instant application is a Continuation of PCT/US04/16419, rather than a 371 of PCT/US04/16419. The case was originally submitted under 35 U.S.C. 371 on 11/19/05 and was accepted under 35 U.S.C. 371 and 37 CFR 1.495 as indicated in the Notice mailed on 5/3/07.

Applicants' responses (10/29/09 and 8/2/10) do not contain any reference to this objection to the ADS. Applicants have not filed a corrected ADS.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4, 6 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Bjorkegren et al (2000. Circulation. 101: 227-230; reference CB on the 11/19/05 IDS). This rejection was set forth previously at pg 6-7 of the 4/30/09 Office Action.

Applicants' arguments (10/29/09; pg 5) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that Bjorkegren et al teach that "subjects having early asymptomatic atherosclerosis have ApoCI-enriched VLDL particles" but do "not teach or suggest that increased levels of ApoCI protein in a biological sample are indicative that the subject is at increased risk for developing atherosclerosis-associated plaque rupture or myocardial infarction, as currently claimed" (pg 5).

Applicants' arguments have been fully considered but are not found persuasive. As set forth previously (pg 6), the 14 CAD patients examined by Bjorkegren et al were all "myocardial infarction survivors" (pg 227). Myocardial infarction survivors inherently have some degree of "risk for developing atherosclerosis-associated plaque rupture" and "myocardial infarction". For evidence of this inherency, Flapan et al teach, "almost half of all survivors of acute myocardial infarctions died or suffered a further ischaemic event within three years" (pg 1129 of Flapan et al, 1994. BMJ. 309: 1129-1134; cited here solely to support inherency). In the amended claims, Applicants have modified the "risk" by adding the word "increased", such that the increased level of ApoCI in the test sample as compared to the control sample indicates that the subject is at increased risk for developing atherosclerosis-associated plaque rupture or myocardial infarction. This change does not patentably distinguish the claimed method from the method taught by Bjorkegren et al. As set forth in the rejection, Bjorkegren found increased ApoCI in the 14 CAD patients as compared to 14 control subjects without CAD. The 14 CAD patients

that are myocardial infarction survivors would inherently have "increased risk for developing atherosclerosis-associated plaque rupture" and "myocardial infarction" as compared to 14 control subjects without CAD, as evidenced by the teachings of Flapan et al (cited above).

Applicants further argue that Bjorkegren et al demonstrate "that increased ApoCI is associated with VLDL" and conclude that "early asymptomatic atherosclerosis in normolipidic men without exaggerated postprandial triglyceridemia is associated with the enrichment of postprandial chylomicron VLDL articles [sic, assumed "particles"] with ApoCI" and "Bjorkegren et al do not teach or suggest increased ApoCI associated with HDL as set forth in new claim 39" (pg 5).

Applicants' arguments have been fully considered but are not found persuasive. Claim 39 is not included in this rejection. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., measuring the level of ApoCI-enriched HDL) are not recited in the rejected claim(s), claims 1, 4, 6 and 8. Furthermore, nothing in the rejected claims excludes increased ApoCI associated with VLDL. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants further argue that Bjorkegren et al "only evaluate a population of male subjects, not female subjects as currently elected" (pg 5).

Applicants' arguments have been fully considered but are not found persuasive. It is not disputed that Bjorkegren et al only provide teachings regarding male subjects. Dependent claim 5, limited to a subject that is female, is not included in this rejection. However, while the currently elected species of subject is a female subject, claims 1, 4, 6 and 8 broadly encompass any human subject, and are thus this genus is subject to rejection as anticipated by the teachings of Bjorkegren et al.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicants are advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bjorkegren et al (2000. Circulation. 101: 227-230; reference CB on the 11/19/05 IDS), as applied to claim 1 above, and further in view of McNamara et al (2001. Atherosclerosis. 154: 229-236; cited previously). This rejection was set forth at pg 9-10 of the 4/30/09 Office Action.

Applicants' arguments (10/29/09; pg 6) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants advance the same arguments against Bjorkegren et al as for the rejection of parent claim 1 under 35 U.S.C. 102(b) ("As indicated above, Bjorkegren et al et al. do not teach or suggest the claimed methods"). Applicants further argue that "the teachings of McNamara et al. do not remedy the deficiencies of Bjorkegren et al" (pg 6).

Applicants' arguments have been fully considered but are not found persuasive. Applicants' arguments against the rejection of parent claim 1 under 35 U.S.C. 102(b) as anticipated by Bjorkegren et al are not persuasive for the reasons described above, and the rejection is maintained. Therefore, the rejection of claim 5 under 35 U.S.C. 103(a)

as being unpatentable over Bjorkegren et al (2000) as applied to claim 1 above, and further in view of McNamara et al (2001) is maintained for the reasons of record.

Claim Rejections - 35 USC § 102/103

Claims 2 and 3 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Bjorkegren et al (2000. Circulation. 101: 227-230; reference CB on the 11/19/05 IDS). This rejection was set forth at pg 11-12 of the 4/30/09 Office Action.

Claim 2 depends from claim 1 and as amended now recites "wherein the ApoCI protein is associated with large HDL". This claim is indefinite for the reasons set forth in the section titled "Claim Rejections - 35 USC § 112, 2nd paragraph" but has been interpreted to encompass a method that measures the level of ApoCI in a biological sample, wherein any of the measured ApoCI protein is associated with large HDL. Claim 3 depends from claim 2 and further recites that "the large HDL levels are elevated".

Claim 2 does not require that the practitioner of the claimed method actually determine that any of the ApoCI protein is associated with large HDL; instead the claim only requires that the ApoCI protein is associated with large HDL. Such encompasses the method of claim 1 wherein the subject in which ApoCI protein is measured inherently has some ApoCI protein associated with large HDL. Likewise, dependent claim 3 does not require that the practitioner measure the large HDL levels. Thus, such encompasses the method of claim 2 wherein the subject in which ApoCI protein is measured inherently has some ApoCI protein associated with large HDL, and wherein the subject inherently has elevated large HDL levels.

As described above, Bjorkegren et al teach a method that anticipates claim 1. Bjorkegren et al do not measure whether or not the subjects have any ApoCI protein associated large HDL as recited in amended claim 2, or whether "the large HDL levels are elevated" as recited in amended claim 3. As taught by the instant specification, "large HDL" is a specific category HDL, for example with a "mean diameter of 11.6 nm" (¶ 214 of the published application).

The examiner is unable to determine whether the subjects used in the prior art (Bjorkegren et al) inherently also have any ApoCI protein associated with large HDL as recited in claim 2, and if so, whether they also have elevated large HDL levels. If said subjects do inherently have some the ApoCI protein associated with large HDL, then the teachings of Bjorkegren et al meets the limitations of claim 2. If said subjects inherently have elevated large HDL levels, then the teachings of Bjorkegren et al also meet the limitations of claim 3.

With these conditions, where a method seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Applicants' arguments (10/29/09; pg 6) as they pertain to the rejection have been fully considered but are not deemed to be persuasive for the following reasons.

In the response, Applicants argue that claim 2 has been amended, "thereby making it clear what is being measured" (pg 6). Applicants argue that "the subject matter of claim 2 is not taught or suggested by Bjorkegren et al. nor is it obvious" (pg 6).

Applicants' arguments have been fully considered but are not found persuasive. Claim has been amended, but does not require any particular measurement. Instead, the claim merely requires that "the ApoCI protein is associated with large HDL". This recitation is indefinite for the reasons set forth in the section titled "Claim Rejections - 35 USC § 112, 2nd paragraph" but has been interpreted to encompass a method that measures the level of ApoCI in a biological sample, wherein any of the measured ApoCI protein is associated with large HDL. The rejection of amended claims 2 and 3 is maintained for the reasons described above.

New rejections necessitated by Applicants' amendment

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-6, 8 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation “the control sample” in line 8. There is insufficient antecedent basis for this limitation in the claim. Specifically, line 6 of claim 1 refers to "the level of ApoCI from a control" rather than a "control sample".

Claim 2 is indefinite because it is unclear how the amended claims limits the method of parent claim 1. In claim 1, a level of ApoCI protein in a biological sample is measured. Claim 2 has been amended to recite that "the ApoCI protein is associated with large HDL levels". It is unclear whether claim 2 limits the method of claim 1 to (1) a method that only measures the level of ApoCI that is associated with large HDL; or (2) a method that measures ApoCI, and some or all of it has an association with large HDL. For purposes of prosecution, the claim is interpreted to read on all of these possibilities.

Claim 3 recites the limitation “the large HDL levels are elevated” in lines 1-2. There is insufficient antecedent basis for this limitation in the claim. Specifically, as amended parent claim 2 refers to "large HDL" rather than "large HDL levels".

Claim 39 recites the limitation “the control sample” in line 8. There is insufficient antecedent basis for this limitation in the claim. Specifically, line 6 of claim 1 refers to "the level of ApoCI-enriched HDL from a control" rather than a "control sample".

The remaining claims are rejected for depending from an indefinite claim.

New Objections

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The Declaration filed on 11/30/06 is defective for the following reasons. In this declaration, the name of one of the inventors is spelled "Peter O. Kwiterowich".

However, in the ADS filed on 11/30/06, the name of the same inventor is spelled "Peter O. Kwiterovich". The same name appears as "Peter O. Kwiterovich" in the published literature (e.g., Kwiterovich et al, 2005. JAMA. 293(15): 1891-1899; cited in the 4/30/09 Office Action). Thus, it would appear that the inventors name is misspelled in the 11/30/06 Declaration. As set forth in 37 CFR § 1.76(d)(3), "[t]he oath or declaration under § 1.63 or § 1.67 governs inconsistencies with the application data sheet in the naming of inventors (§ 1.41 (a)(1)) and setting forth their citizenship (35 U.S.C. 115)". Thus, the ADS filed on 11/30/06 is not sufficient to correct the spelling of the inventor's name; Applicants must submit a corrected Declaration.

Conclusion

No claims are allowed.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicants are reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Bridget E Bunner/
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